4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2013-D-1039]

Draft Guidance for Industry on Endocrine Disruption Potential of Drugs: Nonclinical Evaluation; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled "Endocrine Disruption Potential of Drugs: Nonclinical Evaluation." This draft guidance provides recommendations to sponsors on the parameters that should be routinely assessed in toxicology studies for investigational new drug applications (INDs), new drug applications (NDAs), and biologics license applications (BLAs) regulated by the Center for Drug Evaluation and Research to determine the potential for a drug to disrupt the endocrine system. This draft guidance also discusses factors to consider in determining the need for additional studies to characterize potential endocrine disruptor properties of a drug.

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration,

10903 New Hampshire Ave., Bldg. 51, rm. 2201, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

Submit electronic comments on the draft guidance to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: David Jacobson-Kram, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, rm. 6488, Silver Spring, MD 20993-0002, 301-796-0175.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled "Endocrine Disruption Potential of Drugs: Nonclinical Evaluation." Endocrine disruptors are compounds that have the potential to interfere with some aspect of the endocrine system of an organism or its progeny. Any component of the endocrine system can be a target of endocrine disruptors, although the systems most commonly affected include the sex hormones (e.g., estrogen and androgen), the hypothalamic-pituitary-adrenal axis, the thyroid hormone, and the hormones involved in the feedback regulation of those components (e.g., gonadotropin releasing hormone and corticotropin). Changes in endocrine function can result in transgenerational effects (e.g., through epigenetic mechanisms). Epigenetic modifications are heritable changes in gene function that occur in the absence of changes to the nucleotide sequence. Because such changes

can be maintained and transmitted through the germ cells, these modifications can affect gene actions across generations.

This draft guidance provides recommendations to sponsors on the parameters that should be routinely assessed in toxicology studies for INDs, NDAs, and BLAs that are designed to determine the potential for a drug to disrupt the endocrine system. This draft guidance also discusses factors that should be considered in determining the need for additional studies to characterize potential endocrine disruptor properties of a drug.

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the Agency's current thinking on nonclinical evaluation of endocrine disruption potential of drugs. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

II. Paperwork Reduction Act of 1995

This draft guidance refers to previously approved collections of information that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). The collections of information in 21 CFR parts 312 and 314 have been approved under OMB control numbers 0910-0014 and 0910-0001, respectively.

III. Comments

Interested persons may submit either electronic comments regarding this document to http://www.regulations.gov or written comments to the Division of Dockets Management (see ADDRESSES). It is only necessary to send one set of comments. Identify comments with the

docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at http://www.regulations.gov.

IV. Electronic Access

Persons with access to the Internet may obtain the document at either http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm or http://www.regulations.gov.

Dated: September 16, 2013.

Leslie Kux,

Assistant Commissioner for Policy.

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